



REDUCING NICOTINE IN CIGARETTES WILL REDUCE ADDICTION AND SAVE LIVES

The 2009 Family Smoking Prevention and Tobacco Control Act (“Tobacco Control Act”) gave the U.S. Food & Drug Administration (FDA) regulatory authority over tobacco products, including the ability to require tobacco companies to reduce (but not completely eliminate) the nicotine content of cigarettes. In July 2017, FDA Commissioner Scott Gottlieb announced the agency’s intention to pursue regulation that would reduce nicotine content in cigarettes, and in March 2018 the FDA issued an Advanced Notice of Proposed Rulemaking entitled “Tobacco Product Standard for Nicotine Level of Combusted Cigarettes” to solicit information to guide the development of a nicotine-reduction product standard.¹ The FDA estimates that this proposal would prevent more than 33 million youth and young adults from becoming regular smokers this century, prompt 5 million smokers to quit within one year (rising to 13 million in five years) and save more than 8 million lives by the end of the century.²

For decades, researchers have agreed that nicotine is the fundamental addictive agent in tobacco, leading the U.S. Surgeon General to affirmatively conclude in the 1988 report, *The Health Consequences of Smoking: Nicotine Addiction*, that, “**nicotine is the drug in tobacco that causes addiction.**”³ Now, strong scientific evidence also demonstrates that reducing the nicotine content in cigarettes to a very low level can reduce smoking and nicotine addiction.⁴ Therefore, reducing nicotine levels in cigarettes provides enormous potential to accelerate progress in preventing and reducing smoking and the death and disease it causes.

Tobacco use remains the leading cause of preventable death and disease in the United States. More than 480,000 Americans die from tobacco use each year, and 16 million Americans are currently living with a tobacco-caused disease.⁵ Nearly 38 million Americans currently smoke and every day about 2,300 kids try their first cigarette and another 350 additional kids become regular smokers.⁶ Approximately half of continuing smokers will die prematurely as a result of their addiction, losing at least a decade of life on average compared to nonsmokers.⁷ Making cigarettes minimally or non-addictive will prevent most kids from ever becoming regular smokers and will increase the number of smokers who make a quit attempt and successfully quit.

Nicotine is Highly Addictive

As stated by a Philip Morris researcher in 1972, “**No one has ever become a cigarette smoker by smoking cigarettes without nicotine.**”⁸ Nicotine is the primary addictive agent in cigarettes.⁹ According to the U.S. Surgeon General, “the addiction caused by the nicotine in tobacco smoke is critical in the transition of smokers from experimentation to sustained smoking and, subsequently, in the maintenance of smoking for the majority of smokers who want to quit.”¹⁰ Most adult smokers want to quit (nearly 70 percent) and wish they never started (about 90 percent), but overcoming an addiction to nicotine is difficult and often requires multiple quit attempts before succeeding.¹¹

For most smokers, smoking initiation was not an adult choice but a youthful mistake with serious, long-term consequences for their health. Tobacco use almost always begins during adolescence and adolescents are particularly vulnerable to the addictive effects of nicotine because the brain continues to develop until about age 25. Because adolescence and young adulthood are critical periods of growth and development, exposure to nicotine may have lasting, adverse consequences on brain development.¹² The parts of the brain most responsible for decision making, impulse control, sensation seeking, and susceptibility to peer pressure continue to develop and change through young adulthood.¹³ As a result, nicotine exposure during adolescence may result in impaired attention and memory, problems with learning, reduced self-control and anxiety.¹⁴ Nicotine not only harms the adolescent brain, but is critical to the progression to regular smoking behavior, reinforcing a behavior that exposes smokers to the harmful chemicals responsible for tobacco-related death and disease.

Public Health Impact of Reducing Nicotine in Cigarettes

Reducing the nicotine content in cigarettes to minimally or non-addictive levels will prevent young people who experiment with cigarettes from becoming addicted to cigarettes and save them from a lifetime of addiction and tobacco-caused disease. It also will reduce the level of nicotine dependence in adult smokers, making it easier for them to quit. Most smokers want to quit smoking and reducing the nicotine in cigarettes gives them a much better chance of succeeding. For smokers who are not able to or do not want to quit nicotine use altogether, reducing the nicotine content of cigarettes could prompt them to switch to alternative sources of nicotine that are less dangerous than cigarettes. Ultimately, this will dramatically reduce the number of adult smokers.

As a result, the FDA estimates that reducing nicotine levels in combusted tobacco products would prevent more than 33 million youth and young adults from initiating regular smoking. In addition, within five years, the FDA estimates it would cause 13 million smokers to quit, including five million within just the first year of implementation. Ultimately, more than 8 million lives would be saved by the end of the century.¹⁵

Reducing the nicotine content of cigarettes will not render cigarettes harmless; in fact, products with lower nicotine levels will remain harmful and deadly. While nicotine is the primary addictive agent in cigarettes, the overwhelming health consequences of smoking come from the more than 7,000 chemicals and 69 cancer-causing agents produced from combusted cigarettes.¹⁶

Research Demonstrates that Reducing Nicotine Levels Hold Promise for Reducing Smoking

Research demonstrates that significantly reducing nicotine levels holds great promise for accelerating progress in reducing smoking. Scientific evidence establishes that it is possible to lower nicotine levels in ways that dramatically reduce dependence.

- The first large scale clinical trial of reduced nicotine cigarettes, funded by the FDA and the National Institutes of Health (NIH), was conducted in 2013-2014. The study randomly assigned over 800 smokers to use their usual brand of cigarettes or cigarettes with varying levels of nicotine for six weeks. Smokers assigned to smoke cigarettes with lower nicotine content smoked fewer cigarettes, reduced their exposure and dependence to nicotine, and reduced cravings, compared to the control group.¹⁷
- The same study also found that those smoking cigarettes with the lowest nicotine content (0.4 mg) were twice as likely to report trying to quit in the 30 days after the study ended compared to those smoking cigarettes with 15.8 mg per gram (34% vs. 17%). This is an important finding given that the study excluded smokers who intended to quit within 30 days.¹⁸
- This study bolsters previous research from smaller studies showing that use of reduced nicotine cigarettes leads to outcomes including reduced smoking, nicotine dependence, and biomarkers of exposure to nicotine and other toxins.¹⁹ Other research also shows that reduced nicotine cigarettes increase abstinence among smokers trying to quit.²⁰
- Based on a comprehensive review of the evidence, the World Health Organization Study Group on Tobacco Product Regulation concluded that reducing nicotine content in cigarettes could:²¹
 - Reduce smoking acquisition and progression to addiction;
 - Increase cessation and reduce relapse; and, ultimately,
 - Reduce smoking prevalence.

Research suggests that there would be greater health benefits from implementing a nicotine reduction standard immediately, rather than gradually lowering nicotine levels in cigarettes. A study published in the *Journal of the American Medical Association* in 2018 randomly assigned over 1,000 smokers to normal nicotine content cigarettes, reduced nicotine content cigarettes (0.4 mg/g), or cigarettes with the nicotine content gradually reduced over the course of the study (from 15.8 mg/g to 0.4 mg/g). After twenty weeks, the study found that smokers assigned to the immediate reduction condition showed lower levels of exposure to carbon monoxide and other biomarkers of smoke exposure, compared to the gradual

reduction and control groups. Those in the immediate reduction group also smoked fewer cigarettes per day, were abstinent for longer durations and reported lower levels of nicotine dependence.²²

One potential concern about reducing the nicotine level in cigarettes is that smokers may smoke more cigarettes or inhale smoke more deeply in order to obtain the nicotine fix they are accustomed to (“compensatory smoking”), which would have the unintended consequence of exposing them to even more harmful constituents. However, research to date shows that smokers in fact do not compensate in this manner when nicotine content is reduced to very low levels, particularly when the reduction is immediate rather than gradually stepped down.²³ Substantially reducing nicotine in the tobacco of cigarettes makes it almost impossible to compensate for these lower nicotine levels by smoking more cigarettes, taking more puffs on the cigarette, or inhaling more deeply.

Ethically, it is not possible to conduct the studies necessary to assess the impact of reduced nicotine cigarettes on non-smokers, including adolescents who have never smoked, who may experiment with reduced nicotine cigarettes if made available. However, a recent animal study demonstrated that the same dose of nicotine sufficient to minimize addiction in adult rats is sufficient to prevent addictive behavior in adolescent rats.²⁴ When determining a nicotine reduction threshold, FDA should seek a level that reduces the likelihood that experimentation will create and sustain addiction among experimenters.

Reducing Nicotine in Cigarettes is Technologically Feasible

Research demonstrates that reducing nicotine content in cigarettes to minimally or non-addictive levels is technologically feasible. Further, there is a wide range of techniques available to reduce nicotine content. Tobacco farmers and cigarette manufacturers can reduce the nicotine content of cigarette tobacco by using existing lower-nicotine tobacco plant varieties, creating new plant varieties through genetic manipulation, using tobacco leaves from certain parts of the plant which contain lower nicotine content, or using extraction technology to remove nicotine from tobacco during the manufacturing process.²⁵ In fact, tobacco companies have already demonstrated their proficiency in reducing the nicotine level of cigarettes.* In the 1980s-1990s, Philip Morris produced three brands of low-nicotine cigarettes: Merit De-Nic, Benson & Hedges De-Nic and Next. Vector Tobacco introduced Quest, a low-nicotine cigarette, in 2003. These products, competing in a marketplace dominated by higher nicotine cigarettes, were discontinued due to low consumer demand. The tobacco manufacturer, 22nd Century, currently produces Spectrum, a very low nicotine U.S.-grown tobacco cigarette, which is currently used in government-funded clinical research studies.

Reducing nicotine content in cigarettes to minimally or non-addictive levels is also consistent with several tobacco companies’ purported missions of shifting away from combustible tobacco products by “transforming tobacco” (R.J. Reynolds)²⁶ and investing in a “smoke-free future” (Philip Morris).²⁷

The tobacco industry’s own documents show that the industry also has a long history of manipulating nicotine levels in cigarettes to make them *more* addictive. As U.S. District Judge Gladys Kessler concluded in her landmark 2006 civil racketeering judgment against the major cigarette manufacturers, U.S. v. Philip Morris, Inc., **“Defendants have designed their cigarettes to precisely control nicotine delivery levels and provide doses of nicotine sufficient to create and sustain addiction.”**²⁸ It is clear that the tobacco industry is no stranger to nicotine-manipulation strategies.

Reducing Nicotine Content in Cigarettes Must be Part of a Comprehensive Tobacco Control Effort

A policy to reduce the nicotine level in cigarettes must be viewed as part of a comprehensive tobacco control effort. Tobacco cessation efforts, including mass media campaigns and increased coverage of and access to cessation resources, will be critical. Increased investment in cessation will be needed to provide smokers with the support they need to end their addiction and accommodate the increased volume of smokers attempting to quit. Research also suggests that dual use of reduced nicotine

* Cigarettes with reduced nicotine are often referred to as reduced-nicotine cigarettes, very low nicotine content (VLNC) cigarettes, and de-nicotinized cigarettes.

cigarettes and the nicotine patch yields greater smoking reductions than reduced nicotine cigarettes alone, making it even more important to increase access to cessation.²⁹

Critical to the success of a nicotine reduction policy is a rigorous and comprehensive post-market surveillance and product testing program to monitor for any unintended tobacco use patterns and to identify any changes in product design that may limit the effectiveness of reduced nicotine content.

Studies of adult smokers have shown that they perceive lower nicotine cigarettes to be less harmful than average cigarettes, incorrectly linking nicotine content with risk for smoking-related disease.³⁰ It is critical for the FDA to carefully regulate the marketing of these products, and precede a nicotine reduction policy with public education campaigns to ensure adequate communication about the health risks of these products so as to not encourage non-smokers to experiment. Smokers should be encouraged to quit completely and be educated about the most effective ways to quit successfully.

The impact of reducing nicotine content in cigarettes will be enhanced by the availability of effective cessation treatment and alternative forms of nicotine. Commissioner Gottlieb's proposal to reduce the nicotine content of cigarettes was paired with a directive to the FDA's Center for Drug Evaluation and Research (CDER) to examine mechanisms for improving the performance of existing nicotine replacement therapy and encouraging innovation in medicinal nicotine products. Meeting this directive will enhance the impact of a nicotine reduction policy. Alternative forms of nicotine may be particularly important to help smokers who experience adverse effects or withdrawal symptoms. FDA regulation of new and emerging tobacco products like e-cigarettes is essential to determine which products might help adult smokers quit and remove from the market the most harmful and toxic products and those that encourage initiation among non-smokers, particularly youth.

Some addicted smokers may seek illicit avenues for maintaining their nicotine addiction, rather than quitting. To address this concern, reducing nicotine content in cigarettes should be paired with increased enforcement of manufacturers, wholesalers, and retailers in order to stifle illicit trade, including implementation of a track and trace system. The availability of alternative nicotine products, including nicotine-replacement therapy and non-medicinal nicotine delivery systems, may reduce the likelihood that smokers pursue illicit means for obtaining nicotine.

Finally, extending the proposed nicotine reduction policy to all combustible tobacco products will limit the possibility that cigarette smokers will switch to other dangerous combustible products. History shows that the tobacco industry is adept in manipulating loopholes in tobacco control legislation, and will no doubt promote cigars as alternatives to cigarettes if the policy does not address all forms of combustible tobacco. Cigar smoke contains many of the same harmful constituents as cigarette smoke and may have higher levels of several harmful compounds;³¹ thus, there is no rational basis for reducing nicotine levels in cigarettes, while leaving cigars to remain highly addictive.

Campaign for Tobacco-Free Kids, September 13, 2018 / Laura Bach

¹ U.S. Food and Drug Administration (FDA) Center for Tobacco Products, "FDA announces comprehensive regulatory plan to shift trajectory of tobacco-related disease, death," July 28, 2017, <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm568923.htm>.

² Apelberg, B.J., et al., "Potential Public Health Effects of Reducing Nicotine Levels in Cigarettes in the United States," *New England Journal of Medicine*, published online March 15, 2018. See also Tobacco Product Standard for Nicotine Level of Combusted Cigarettes; Advanced Notice of Proposed Rulemaking, 83 Fed. Reg. at 11818 (March 16, 2018).

³ U.S. Department of Health and Human Services (HHS). The Health Consequences of Smoking: Nicotine Addiction. A Report of the Surgeon General. Atlanta (GA): U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 1988. DHHS Publication No. (CDC) 88-8406.

⁴ World Health Organization (WHO) Study Group on Tobacco Product Regulation, *Global Nicotine Reduction Strategy*, 2015, http://apps.who.int/iris/bitstream/10665/189651/1/9789241509329_eng.pdf?ua=1.

⁵ HHS, *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General*, 2014, <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>.

⁶ Centers for Disease Control and Prevention (CDC), "Current Cigarette Smoking Among Adults – United States, 2016," *Morbidity and Mortality Weekly Report (MMWR)* 67(2):53-59, January 19, 2018. <https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6702a1-H.pdf>; Substance Abuse and Mental Health Services Administration (SAMHSA), HHS, *Results from the 2016 National Survey on Drug Use and Health, NSDUH: Detailed Tables*, 2017. <https://www.samhsa.gov/data/sites/default/files/NSDUH-DeTTab-2016/NSDUH-DeTTab-2016.pdf>.

⁷ HHS, *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General*, 2014, <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>.

⁸ Philip Morris, Dunn, W Jr., "Motives And Incentives In Cigarette Smoking"; R107. 1972.

<https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/jspf0085>. For additional industry quotes on nicotine, see Campaign for Tobacco-Free Kids fact sheet, "Tobacco Company Quotes: Nicotine as a Drug," <https://www.tobaccofreekids.org/research/factsheets/pdf/0009.pdf>.

⁹ HHS, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General*, 2010, <http://www.ncbi.nlm.nih.gov/books/NBK53017/>.

¹⁰ HHS, *The Health Consequences of Smoking—50 Years of Progress, A Report of the Surgeon General*, 2014,

<http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>. See also, HHS, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General*, 2010, <http://www.ncbi.nlm.nih.gov/books/NBK53017/>.

¹¹ Babb, S, et al., "Quitting Smoking Among Adults—United States, 2000—2015," *MMWR* 65:1457–1464, 2017. Fong, G., et al., "The Near-Universal Experience of Regret Among Smokers in Four Countries: Findings from the International Tobacco Control Policy Evaluation Survey," *Nicotine & Tobacco Research*, Vol. 6, Supplement 3, December 2004.

¹² HHS. *The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General*, 2014; Institute of Medicine, *Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products*, Washington, DC: The National Academies Press, 2015, <http://iom.nationalacademies.org/Reports/2015/TobaccoMinimumAgeReport.aspx>

¹³ Institute of Medicine, *Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products*, Washington, DC: The National Academies Press, 2015.

¹⁴ England, L.J, et al., "Nicotine and the Developing Human: A Neglected Element in the Electronic Cigarette Debate." *American Journal of Preventive Medicine*, 2015; Gorionova NA, Mansvelder HD, "Short-and Long-Term Consequences of Nicotine Exposure During Adolescence for Prefrontal Cortex Neuronal Network Function," *Cold Spring Harbor Perspectives in Medicine*, 2012; Steinberg, Laurence, "Should the Science of Adolescent Brain Development Inform Public Policy?," *Issues in Science and Technology*, Volume XXVIII, Issue 3, Spring 2012.

¹⁵ Apelberg, B.J, et al., "Potential Public Health Effects of Reducing Nicotine Levels in Cigarettes in the United States," *New England Journal of Medicine*, published online March 15, 2018. See also Tobacco Product Standard for Nicotine Level of Combusted Cigarettes; Advanced Notice of Proposed Rulemaking, 83 Fed. Reg. at 11818 (March 16, 2018).

¹⁶ HHS, *The Health Consequences of Smoking—50 Years of Progress, A Report of the Surgeon General*, 2014, <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>.

¹⁷ Donny, EC, et al., "Randomized trial of reduced-nicotine standards for cigarettes," *New England Journal of Medicine*, 373: 1340-1349, 2015.

¹⁸ Donny, EC, et al., "Randomized trial of reduced-nicotine standards for cigarettes," *New England Journal of Medicine*, 373: 1340-1349, 2015.

¹⁹ See e.g., Donny EC, Houtsmuller E, Stitzer ML. Smoking in the absence of nicotine: behavioral, subjective and physiological effects over 11 days. *Addiction* 2007; 102: 324-34. Benowitz NL, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P III. Nicotine and carcinogen exposure with smoking of progressively reduced nicotine content cigarette. *Cancer Epidemiol Biomarkers Prev* 2007; 16: 2479-85. Benowitz NL, Dains KM, Dempsey D, Herrera B, Yu L, Jacob P III. Urine nicotine metabolite concentrations in relation to plasma cotinine during low-level nicotine exposure. *Nicotine Tob Res* 2009; 11: 954-60. Benowitz NL, Dains KM, Hall SM, et al. Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes. *Cancer Epidemiol Biomarkers Prev* 2012; 21: 761-9. Hatsukami DK, Hertsgaard LA, Vogel RI, et al. Reduced nicotine content cigarettes 9. Donny EC, Houtsmuller E, Stitzer ML. Smoking in the absence of nicotine: behavioral, subjective and physiological effects over 11 days. *Addiction* 2007; 102: 324-34. Benowitz NL, Hall SM, Stewart S, Wilson M, Dempsey D, Jacob P III. Nicotine and carcinogen exposure with smoking of progressively reduced nicotine content cigarette. *Cancer Epidemiol Biomarkers Prev* 2007; 16: 2479-85. Benowitz NL, Dains KM, Dempsey D, Herrera B, Yu L, Jacob P III. Urine nicotine metabolite concentrations in relation to plasma cotinine during low-level nicotine exposure. *Nicotine Tob Res* 2009; 11: 954-60. Benowitz NL, Dains KM, Hall SM, et al. Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes. *Cancer Epidemiol Biomarkers Prev* 2012; 21: 761-9. Hatsukami DK, Hertsgaard LA, Vogel RI, et al. Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation. *Addiction* 2010; 105: 343-55.

²⁰ See e.g., Walker, N, et al., "The combined effect of very low nicotine content cigarettes, used as an adjunct to usual Quitline care (nicotine replacement therapy and behavioural support), on smoking cessation: a randomized controlled trial," *Addiction*, 107(10): 1857-1867, 2012. McRobbie, H, et al., "Complementing the standard multicomponent treatment for smokers with denicotinized cigarettes: a randomized controlled trial," *Nicotine & Tobacco Research*, 18(5): 1134-1141, 2016.

²¹ World Health Organization (WHO) Study Group on Tobacco Product Regulation, *Global Nicotine Reduction Strategy*, 2015, http://apps.who.int/iris/bitstream/10665/189651/1/9789241509329_eng.pdf?ua=1.

²² Hatsukami, DH, et al., "Effect of Immediate vs. Gradual Reduction in Nicotine Content of Cigarettes on Biomarkers of Smoke Exposure: A Randomized Clinical Trial," *JAMA*, 320(9): 880-891, 2018.

²³ See e.g., Donny, EC, et al., "Randomized trial of reduced-nicotine standards for cigarettes," *New England Journal of Medicine*, 373: 1340-1349, 2015. Hatsukami, DK, et al., "Compensatory smoking from gradual and immediate reduction in cigarette nicotine content," *Cancer Epidemiology, Biomarkers & Prevention*, 24: 472-476, 2015. Benowitz, NL, et al., "Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes," *Cancer Epidemiology, Biomarkers & Prevention*, 21: 761-769, 2012. Hatsukami, DK, et al., "Nicotine reduction revisited: science and future directions," *Tobacco Control*, 19: e1-10, 2010. Hatsukami, DK, et al., "Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation," *Addiction*, 105: 343-355, 2010.

²⁴ See e.g., Schassburger, RL, et al., "Adolescent rates self-administer less nicotine than adults at low doses," *Nicotine & Tobacco Research*, 15: 1003-1013, 2016. Smith, TT, et al., "Animal research on nicotine reduction: current evidence and research gaps," *Nicotine & Tobacco Research*, published online April 4, 2017.

²⁵ Tengs, T.O., et al., "The AMA proposal to mandate nicotine reduction in cigarettes: a simulation of the population health impacts," *Preventive Medicine*, 40: 170-180, 2005.

²⁶ RJ Reynolds, "Our vision: We will achieve market leadership by transforming the tobacco industry," accessed August 8, 2017, <http://www.rjrt.com/transforming-tobacco/our-mission-and-vision/>.

²⁷ Philip Morris, "Our Manifesto: Designing a Smoke-Free Future," Accessed August 8, 2017, <https://www.pmi.com/who-we-are/designing-a-smoke-free-future>.

²⁸ U.S. v. Philip Morris, USA, Inc., 449 F. Supp. 2d (D.D.C. 2006) at 309.

²⁹ Hatsukami, DK, et al., "Reduced nicotine content cigarettes and nicotine patch," *Cancer Epidemiology, Biomarkers & Prevention* 22(6): 1015-1024, 2013. Donny, EC, et al., "Prolonged exposure to denicotinized cigarettes with or without transdermal nicotine," *Drug & Alcohol Dependence*, 104(1-2): 23-33, 2009.

³⁰ See e.g., Denlinger-Apte, RL, et al., "Low nicotine content descriptors reduce perceived health risks and positive cigarette ratings in participants using very low nicotine content cigarettes," *Nicotine & Tobacco Research*, published online January 18, 2017. Pacek, LR, et al., "Perceived nicotine content of reduced nicotine content cigarettes is a correlate of perceived health risks," *Tobacco Control*, published online July 22, 2017. O'Brien, EK, et al., "U.S. adults' addiction and harm beliefs about nicotine and low nicotine cigarettes," *Preventive Medicine*, 96: 94-100, 2017.

³¹ National Cancer Institute (NCI), *Cigars: Health Effects and Trends. Smoking and Tobacco Control Monograph No. 9*, 1998, http://cancercontrol.cancer.gov/Brp/tcrb/monographs/9/m9_complete.pdf.